

REMARKS/ARGUMENTS

Claims 1-10 are pending in the present case. Claim 1 has been amended to place the claims in better form for allowance. The Examiner is respectfully requested to enter the amendments, consider the remarks below and reconsider the application.

The Examiner has rejected Claims 1-3 under 35 USC §102(e) as being anticipated by Seed, et al. US Pat. No. 5,861,399 citing "line 62 of col. 2 through line 20 of col. 3". The Examiner acknowledges that Seed teaches lowering LDL with a combination of diet and drugs as argued by the Applicants' in the previous response. The Examiner notes that "the claims do not require the exclusion of dietary restriction". Claim 1 has been amended to make it clear that the method itself does not include a dietary treatment component. The language "consisting of" is intended to include treatment of patients without regard for any particular dietary restrictions.

A claim is anticipated only if each and every element as set forth in the claim is found in the prior art reference (see, Verdegaal Bros. v. Union Oil Co. of California, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)). The present claims are directed toward a method for preventing or delaying catheter-based revascularization in patients suffering from coronary artery disease and in need of such treatment consisting essentially of administering a cholesterol lowering agent in an amount effective to cause an aggressive lowering of LDL cholesterol. As acknowledged by the Examiner, Seed does not disclose a method of aggressively lowering LDL using drug alone, "but rather discloses a combination of treatments (drugs and diet)." Therefore, Seed does not disclose each and every element of amended Claim 1, and dependent claims 2 and 3. Applicant therefore requests withdrawal of the rejection under 35 USC §102(e).

Rejections under 35 USC §103(a)

The Examiner has rejected Claims 1-4 and 9-10 under 35 USC §103(a) as being unpatentable over Whitney, et al. US Pat No. 6,180,660 in view of Jeevanandam, et al. US Pat No. 5,957,916. The Examiner states that Whitney et al. discloses in lines 17-43 of col. 1, lines 8-13 of col. 2, 45-51 of col. 4, lines 27-29 of col. 3, Example 1 in col. 5-6, and lines 1-37 of col. 7 a method of administering cholesterol lowering drugs such as atorvastatin or fibrates to prevent or delay the need for coronary revascularization procedures. The Examiner further notes that Whitney, at column 5, lines 29-44 "describe[s] awareness of the 'trend to treat coronary heart disease aggressively before a myocardial infarction has occurred.'"

Applicant disagrees with the Examiner's characterization of this reference. Whitney does not teach or suggest preventing or delaying revascularization in patients suffering from coronary artery disease. The disclosure of Whitney is around the treatment of individuals without coronary artery disease. The clinical trial that is the basis for the Whitney disclosure, the AFCAPS/TexCAPS trial, is limited to "a cohort without clinical evidence of atherosclerotic cardiovascular disease." Entrance inclusion criteria included that the patient's LDL level be 130-190 mg/dl, col. 5, lines 44-45. Indeed as noted by the Examiner, during the trial, patients with LDL levels greater than 195 mg/dl were withdrawn from the trial. The Examiner's statement (office action page 3) that "some may have suffered or did suffer from coronary artery disease" is from a misunderstanding of what Whitney discloses. The Examiner incorrectly attributes disclosure in lines 34-44, col. 6, of Whitney as describing patients in the trial (office action page 3). Col 6, lines 33-36 reads "Excluded [from the trial] for clinical evidence of atherosclerotic cardiovascular disease were men and women who had: prior history of myocardial infarction; . . . " Therefore, the results of Whitney would not have conveyed to one of skill in the art that treatment with a statin could prevent or delay revascularization in patients suffering from coronary artery disease, as is claimed in the present invention – that patient population was simply not studied in Whitney.

The Examiner states that Applicant's disclosure has not fully described what is encompassed by "patients suffering from coronary artery disease." The Applicant respectfully disagrees. One of skill in the art reading the present disclosure would understand that these patients would have evidence of atherosclerotic disease. For example the specification discloses that the patients in the study are those for "whom a recanalization procedure is recommended." page 8, lines 17-18.

Lines 45-51 of col. 4, of Whitney do describe that the invention may be used to prevent or reduce the risk of a first occurrence of a non-fatal cardiovascular event such as a revascularization procedure. However, as discussed above, within the context of the disclosure, when taken as a whole, one of skill in the art would understand this to be limited to individuals with no history of clinically evident coronary heart disease (CHD) prior to the administration of the lipid lowering agent. One of skill in the art would recognize that because the data in Whitney is derived from "a cohort without clinical evidence of atherosclerotic cardiovascular disease," that this data does not equate to a disclosure of a method of preventing or delaying catheter-based revascularization in patients suffering from coronary artery disease.

The Examiner has rejected claims 1-6 under 35 USC §103(a) as being unpatentable over Bocan et al. WO 97/16184 in view of Jeevanandam. The Examiner summarily states "Bocan discloses in lines 12-25 of page 3 and lines 1-12 of page 5 a method of delaying or preventing the need for revascularization in patients suffering from coronary artery [sic] by administering 5-80 mg of atorvastatin per day."

The Applicant disagrees with the Examiner's restatement of the disclosure of Bocan. Nowhere in the disclosure does Bocan disclose the method of the present invention. While Bocan does describe that lipid lowering therapy with HMG-CoA reductase inhibitors normalizes vascular function in patients with hypercholesterolemia and/or coronary artery disease without the requirement for significant regression of the atherosclerotic lesions. This is not the same as disclosing that treatment with a cholesterol lowering agent can prevent or delay catheter based revascularization. At best it might make the present invention obvious to try. Bocan cannot render the present invention obvious because it does not provide an expectation of success. Bocan only has data concerning lipid reduction in animals. Bocan does not disclose any data on prevention or delay of catheter-based revascularization.

One of skill in the art would not have reasonably expected such a method to succeed without reference to data such as is provided by the disclosure of Applicant's application. It is in Applicant's disclosure that the support for prevention or delay of catheter-based revascularization in patients suffering from coronary artery disease is found. Applicant is the first to show that high doses of a cholesterol lowering drug reduce the incidence of an adverse cardiac event from 21% to 13%, thereby decreasing the need for revascularization. (p 25, lines 5-24). To establish a *prima facie* case of obviousness, the reasonable expectation of success must be found in the prior art references not in the Applicant's disclosure.

The Examiner has rejected Claim 1, 7, and 8 under 35 USC §103(a) as being unpatentable over Bisgaier et al. US Pat No. 5,648,387 in view of Jeevanandam et al. US Pat No. 5,957,916.

The Examiner's rejection implies that the method of Bisgaier is the same as that of the instant invention except that it is not taught to prevent the need for catheter-based revascularization. This is simply not the case. The Examiner points to specific sections of the disclosure but these sections simply describe the compound that is the subject of the application and that those compounds are useful for lowering certain plasma lipids in mammals. The Examiner has not pointed to any specific disclosure in Bisgaier in which all elements of Applicant's claimed invention are disclosed. Bisgaier does not teach or suggest administration of an amount of a cholesterol-lowering agent effective to cause an aggressive

lowering of LDL cholesterol. Bisgaier does not teach using an amount of a cholesterol-lowering agent effective to cause an aggressive lowering of LDL cholesterol. Nor does Bisgaier teach or suggest a method for preventing or delaying revascularization

While Bisgaier does, in passing, disclose a method of treating vascular diseases such as restenosis (col. 2, lines 49-51), Applicant would like to point out that treating restenosis is different than preventing or delaying revascularization where there has not been an initial surgical procedure. As discussed in the response to the previous office action, Restenosis refers to the reoccurrence of stenosis in a blood vessel **after** surgical correction of the primary condition (Dorland's Illustrated Medical Dictionary, 29th edition). In other words, restenosis is a treatment-related condition (iatrogenic) associated with catheter injury to the treated vessel and subsequent proliferative cellular reocclusion of the same vessel. Restenosis is **not** the same as indigenous or 'native' coronary atherosclerosis resulting from cholesterol accumulation in the vessel wall. The mechanism of restenosis is different from that of the formation of the original stenosis that necessitated surgical treatment. Restenosis involves a proliferation of smooth muscle cells in the treated artery whereas stenosis (a narrowing of a blood vessel) is thought to involve lipid deposition and the inflammatory response. Thus, Bisgaier does not disclose or suggest a method of preventing or delaying catheter-based revascularization as is claimed in the present invention.

Given the reasons above, Applicant asserts that Claims 1-10 under 35 USC §103(a), would not have been obvious to one of ordinary skill in the art at the time the application was filed, and the Applicant therefore requests withdrawal of this rejection, and allowance of the claims.

Respectfully submitted,

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